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CASE REPORT

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Atypical hemolytic uremic syndrome in a child: A rare case report

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Key Clinical Message

Atypical hemolytic uremic syndrome, a rare thrombotic microangiopathy, necessitates early diagnosis and comprehensive care due to its potential severity, emphasizing the importance of a multidisciplinary approach to improve outcomes.

KEYWORDS

acute kidney injury, atypical hemolytic uremic syndrome, hemolytic anemia, thrombocytopenia, thrombotic microangiopathies

1 | INTRODUCTION

Thrombotic microangiopathy (TMA) is characterized by microvascular thrombosis that causes thrombocytopenia, Coombs-negative hemolytic anemia, and end-organ destruction.[1,2] Atypical hemolytic uremic syndrome (aHUS) is a rare and potentially fatal TMA that affects multiple organ systems.[3]

aHUS is differentiated from hemolytic uremic syndrome (HUS) by not being typically associated with Shiga toxin (Stx)-producing bacteria, typically *Escherichia coli* O157:H7 or any other infection.[4,5] aHUS is associated with a genetic or acquired defect in complement system regulation of host cells.[6] The prevalence of aHUS in the child population with less than 18 years of age is found to be 3.3 per million.[7] aHUS has a poor prognosis with a mortality rate of 25% and up to 50% of cases advance to end-stage renal disease (ESRD).[4,5]

2 | CASE REPORT

Our patient, an 11-year-old male child, developmentally normal, immunized for age presented in the Emergency Department. According to his mother who had good reliability, the child was well 3 days back, when he developed a headache which was of sudden onset, generalized, continuous radiating to the nape of the neck, relieved for 2 h by taking medicine from the local hospital but reappearing. It was associated with a decreased appetite for which vitamin supplements were given which improved his appetite. It was also associated with fever and shortness of breath. He had three episodes of vomiting; moderate in quantity which was non-projectile, non-bilious, non-blood stained, and containing ingested food particles.

On general examination, patient looked drowsy with altered sensorium and other significant findings included clubbing, raised blood pressure (240/150 mm of Hg) and mean arterial pressure of 160 mm of Hg, pulse rate of 134

per minute. On examination of relevant systems, significant findings included soft tender splenomegaly and flow murmur. In triage, the child had an open but unstable airway and normal breathing with a Glasgow Coma Scale of 7/15.

2.1 | Diagnostic assessments

Initially, the child was suspected to have primary brain/systemic dysfunction in the emergency department, computed tomography (CT) of the head was done for suspected intracranial hemorrhage, but the findings were suggestive of posterior reversible encephalopathy syndrome (Figure 1). The airway was secured with intubation and the child was shifted to the pediatrics intensive care unit with a provisional diagnosis of hypertensive emergency with encephalopathy.

Following were the values of laboratory investigation during admission: Hemoglobin (Hb): 5.9 g/dL; packed cell volume (hematocrit): 18.3%; red blood cell (RBC) count: 2.21 million/mm^3, platelets: 81,000/mm^3, prothrombin time (PT): 14.5 s, activated partial thromboplastin time (aPTT): 38.2 s, blood urea: 80.09 mg/dL, creatinine: 2.61 mg/dL, lactate dehydrogenase (LDH): 1023 Units/L and total bilirubin: 1.4 mg/dL.

Peripheral blood smear (PBS) revealed predominantly anisopoikilocytic RBC with frequent schistocytes, helmet cells, and few microcytes suggestive of hemolysis (Figure 2). Urinalysis showed proteinuria (Albumin ++) and hematuria. Microscopic examination of urine revealed pus cells 1–3 per high power field (HPF), epithelial cells 1–3 per HPF, and RBC 4–6 per HPF. Ophthalmology examination revealed Grade III hypertensive retinopathy. Echocardiography was suggestive of left ventricular hypertrophy with a left ventricular ejection fraction of 60%.

Tropical infections were ruled out as there was normal procalcitonin with a malarial parasite (MP) smear and Scrub serology being normal. The patient had negative antinuclear antibody (ANA), Anti-DNA, myeloperoxidase, and proteinase-3 antibody assays ruling out Lupus nephritis and ANCA-associated vasculitis. A comprehensive array of laboratory investigations, including renal function test (RFT), liver function (LFT), thyroid function test (TFT), complete blood count (CBC), aldosterone renin ratio, 24-h urine Vanillylmandelic acid (VMA) collection, coagulation profile analysis, and phospholipid syndrome profile assessment, were conducted extensively. These tests were pivotal in the diagnostic process as they helped exclude other potential causes and narrow down the diagnosis. In addition, other potential causes such as leptospirosis, salmonellosis, shigellosis, Hepatitis B, Hepatitis C, human immunodeficiency virus (HIV), dengue, and streptococcal infections were ruled out from the diagnostic process.

The above-mentioned laboratory findings of thrombocytopenia, microangiopathic hemolytic anemia with increased LDH, and renal dysfunction suspected the patient as a case of typical HUS with acute kidney injury (AKI). However, no growth was seen during blood culture, after 48 h of incubation at 37°C. Hence, the diagnosis of aHUS was confirmed.

2.2 | Treatment

The child was put on mechanical ventilation under sedation with synchronized intermittent mandatory ventilation (SIMV) settings for 3 days and after that, an extubation trial was given which the child tolerated well.

For hypertensive emergency, Labetalol infusion was initially started and titrated to 1 mg/kg/h in the next 48 h to a blood pressure (BP) of 90th centile. Invasive arterial line BP monitoring was done. Gradually there was a fall to near 90th centile following which Labetalol infusion was stopped and was started on oral antihypertensives (Amlodipine & Labetalol, Lasilactone, Clonidine). However, he had frequent episodes of accelerated hypertension for which IV Losartan and oral Enalapril were added.

Initial hemoglobin was 5.9 g/dL for which packed red blood cells (PRBC) transfusion was given following which Hb increased to 7.5 mg/dL after which the child was hemodynamically stable. After numerous discussions and consultations with the physician, the medical team proposed that a renal biopsy be performed on the child. However, the parents were non-compliant and left against medical advice.

3 | DISCUSSION

Clinically, thrombotic thrombocytopenic purpura (TTP) and HUS associated with Shiga toxin-producing Escherichia coli infection (STEC-HUS) are the most often reported TMAs, followed by aHUS and secondary HUS.[8] The discovery of the link between aHUS and mutations in the gene encoding complement factor H (CFH), the primary complement regulator in plasma, signaled the start of the identification of fundamental distinctions in pathophysiology between aHUS and STEC-HUS.[9] Although the defects of the complement system play a central role in the pathophysiology of aHUS, it is crucial to understand that even if levels of complement components C3 and/or C4 are within the normal range, it does not rule out the presence of aHUS.[10] Therefore, it is not advisable to solely rely on complement activation biomarkers for making a definitive diagnosis of aHUS. There

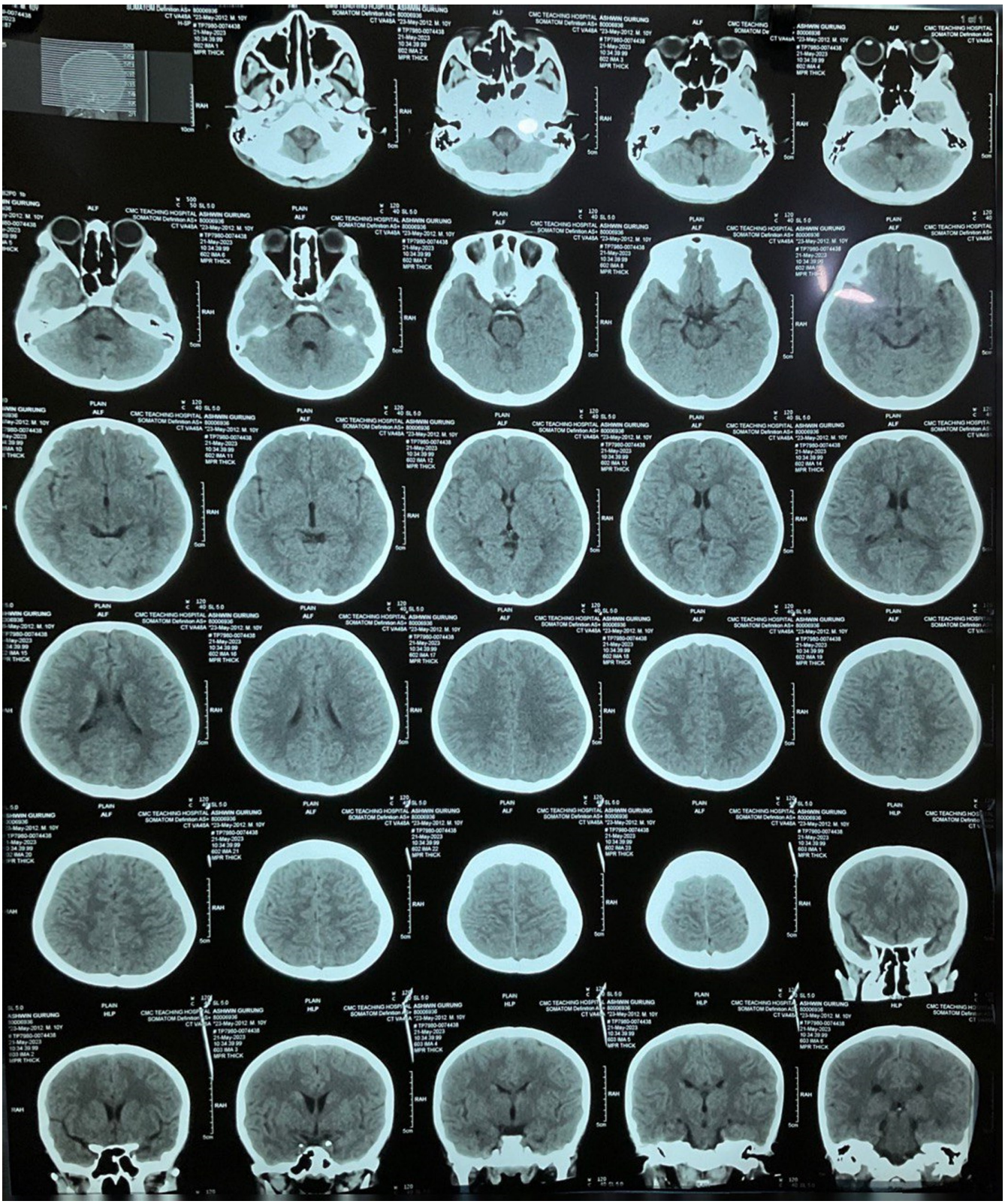

FIGURE 1 Computed tomography of head shows subtle hypodensities in the bilateral occipital lobes (left > right) suggestive of posterior reversible encephalopathy syndrome.

is no elevation in the serum level of C3 and C4 in our patient. There is no elevation of anti-complement Factor H in the patient serum.

With the goal of simplifying early diagnosis and efficient care of this disorder, the Joint Committee of the Japanese Society of Nephrology and the Japan Pediatrics

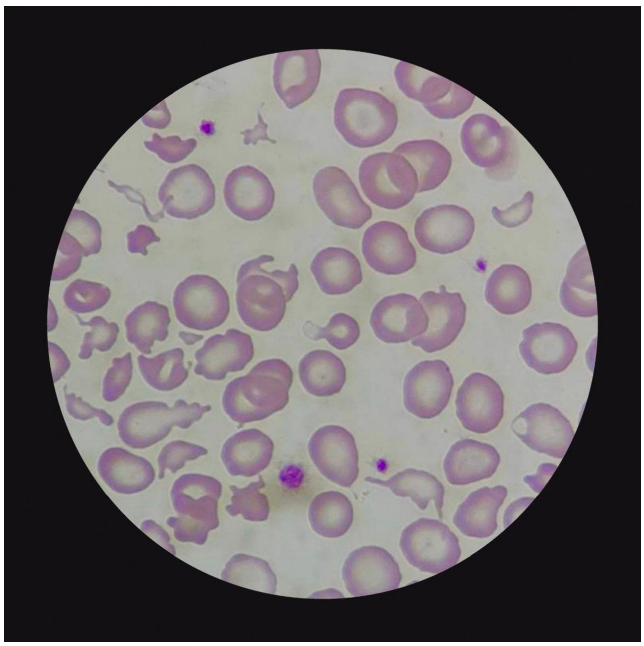

FIGURE 2 Peripheral blood smear shows anisopoikilocytic red blood cells, schistocytes with decreased platelet count.

Society (JSN/JPS) has developed diagnostic criteria for aHUS which includes three crucial clinical features.[11] The first feature is thrombocytopenia, which is characterized by a platelet count below 150,000/μL. The second feature is microangiopathic hemolytic anemia, which manifests as low hemoglobin levels (below 10 g/dL), increased lactate dehydrogenase levels, reduced haptoglobin levels, and the presence of fragmented red blood cells observed in the peripheral blood smear. The third feature is acute renal failure, as defined by the Kidney Disease: Improving Global Outcomes international guidelines.[11] In our case as well, the child is thrombocytopenic, has got severe hemolytic anemia with negative Coombs test, elevated Lactate dehydrogenase along with acute renal injury suggesting the diagnosis of atypical hemolytic uremic syndrome according to the above guidelines.

A targeted therapy to stop and reverse TMA should be used in conjunction with supportive treatment measures to manage the effects of aHUS (such as acute renal failure, high blood pressure, anemia, thrombocytopenia, etc.)[3] Treatment for aHUS is mostly supportive which focuses on managing acute renal damage and systemic consequences. In order to prevent the effects of aHUS, acute kidney injury, and multisystem organ failure, it is crucial to regulate fluid and electrolyte levels. In patients with severe anemia, use of packed cells is necessary. Specific forms of therapy include plasma exchange and the complement inhibitor eculizumab.[12] Complement gene genetic testing is typically advised since it enables personalized prognosis and illness recurrence risk calculations. There has been controversies regarding whether kidney transplantation is appropriate for the treatment of end-stage renal disease in patients with aHUS.[13]

Knowing the approach to diagnose and treat aHUS is essential since early detection and treatment reduce disease morbidity and death.

4 | CONCLUSION

The prognosis of individuals with aHUS can be significantly improved by early recognition and comprehensive management. Multidisciplinary approach is essential for aHUS due to its rarity and potential severity. Hence, further study is needed to enhance knowledge and optimize treatment strategies for this challenging condition.

AUTHOR CONTRIBUTIONS

Bishal Kunwor: Conceptualization; data curation; formal analysis; supervision; validation; visualization; writing – original draft; writing – review and editing. **Bishal Sharma:** Conceptualization; data curation; formal analysis; supervision; validation; visualization; writing – original draft; writing – review and editing. **Suchit Thapa Chhetri:** Conceptualization; data curation; formal analysis; supervision; validation; visualization; writing – original draft; writing – review and editing. **Prerana Joshi:** Formal analysis; validation; visualization; writing – original draft; writing – review and editing. **Dipendra Pradhan:** Validation; visualization; writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

No conflict of interest.

DATA AVAILABILITY STATEMENT

All the findings are present within the manuscript.

CONSENT

Written informed consent form was obtained from the patient to publish this report in accordance with the journal's consent policy.

PATIENT PERSPECTIVE

The family members of the child were anxious about his condition. They were properly counseled and assured that he would get better. However, the patient party left against the medical advice.

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